REMARKS

In response to the Office Action mailed July 13, 2005, Applicants canceled claims 9-13, and amended claims 1-7 and 34-48. No new matter has been added by the amendments. Claims 1-7 and 34-48 are presented for examination.

Information Disclosure Statement

The references requested by the Examiner have been provided with an Information Disclosure Statement accompanying this response. Applicants note, however, that these references (Huang *et al.*, Meurer and Hutchinson, Moche *et al.*, and Olsen *et al.*) were cited in an Information Disclosure Statement and PTO Form-1449 that was initialed by the Examiner in the parent case (U.S.S.N. 09/770,834). As permitted under 37 C.F.R. § 1.98(d), copies of these references were cited in, but not provided with, the Information Disclosure Statement filed with the present application on November 19, 2003.

Compliance with Sequence Rules

The description of Figures 3 and 3A1 to 3A-79 beginning at page 7, line 15 has been amended to reference SEQ ID NO:2 with respect to ACPS and to reference SEQ ID NO:1 with respect to ACP. The description of Figures 5 and 5A-1 to 5A-15 beginning at page 8, line 1 has been amended to reference SEQ ID NO:1 with respect to ACP. The application is believed to comply with the requirements of 37 C.F.R. § 1.821 through § 1.825, and a substitute copy of the sequence listing is not required.

The Examiner has asked for clarification regarding the numbering of amino acid residues in Figure 3A-47 and Figure 5. The amino acid residues in Figure 3A-47 and Figure 5 correspond to the amino acid sequence of ACP shown in Figure 1 (SEQ ID NO:1). The amino acid designated "1" is an alanine (ALA1) and represents the first amino acid of *B. subtilis* ACP. The five amino acids proceeding ALA1 (GPLGS) correspond to the five C-terminal amino acids remaining from a GST tag that was fused to the polypeptide to facilitate ACP purification. Following purification over a glutathione sepharose column, the intact GST-ACP fusion

polypeptide was cleaved with PreScission Protease, leaving the five-amino acid GST fragment fused to ACP. This polypeptide fragment was used for structure determination experiments. The details of this protocol are described at page 26, line 4 through page 27, line 3.

Objections to the Specification

Applicants amended the title and the abstract to address the issues raised by the Examiner.

35 U.S.C. § 112

Indefiniteness. The Examiner rejected claims 2-5 under 35 U.S.C. § 112, second paragraph as being indefinite. Claims 2 and 3 have been amended to clarify that the amino acid residues refer to the amino acids at the positions set forth in SEQ ID NO:2. Claims 4 and 5 have been amended to clarify that the amino acid residues refer to the amino acids at the positions set forth in SEQ ID NO:1.

The Examiner rejected claims 9-13 under 35 U.S.C. § 112, second paragraph as being indefinite. Claims 9-13 have been cancelled by the above amendment, thereby obviating the rejection.

The Examiner rejected claims 9-13, 34-38, and 39-48 under 35 U.S.C. § 112, second paragraph as being indefinite with respect to the recitation that an active site of an acyl carrier protein synthase comprises structural coordinates according to Figure 3 ± a root mean square deviation from the backbone atoms. The Examiner asks at page 6 of the Office Action whether the active sites must contain the specified side chain residues, and if so, then why the backbone atoms of the amino acid residues can deviate from those specified in the figure, and not the atoms of the side chain residues.

The reference to the backbone atoms of a polypeptide, and in this case the backbone atoms of the ACPS and ACP polypeptides included in the crystallized complex of Figures 3 and 3A-1 to 3A-79, is standard in the field of protein crystallography. The polypeptide backbone provides a reference point that is a common structure among all polypeptides regardless of the

amino acid sequence and the associated variable combination of side-chain residues. The reference of the accepted deviation from a deduced structure is typically by reference to the polypeptide backbone, which provides the general shape (*i.e.*, skeleton structure) of the folded polypeptide and is generally less susceptible to deviation. As a person having ordinary skill in the art of protein crystallography would understand the reference to an accepted deviation from a given set of structural coordinates and with respect to the polypeptide backbone, no further clarification is necessary.

Claims 35 and 36 have been amended to indicate that the amino acids referenced in the claims refer to those set forth in SEQ ID NO:2. Claims 37 and 38 have been amended to indicate that the amino acids referenced in the claims refer to those set forth in SEQ ID NO:1. Claims 9-13 have been canceled and therefore the rejection of these claims is moot.

At page 7 of the Office Action, the Examiner states that Figure 3 contains two different amino acid sequences. Claims 2-5 and 35-38 have been amended to clarify that the designated amino acids refer to those set forth in either SEQ ID NO:1 or SEQ ID NO:2. Figures 3 and 3A-1 to 3A-79 show the structural coordinates that were determined by X-ray diffraction from a crystallized complex containing three ACPS and three ACP molecules. The amino acid sequences of each of the three ACPS polypeptides in the crystallized complex are the same (and correspond to SEQ ID NO:2), and the sequences of each of the three ACP polypeptides in the crystallized complex are the same (and correspond to SEQ ID NO:1). However, as the Examiner noted, some of the amino acid residues in Figures 3 and 3A-1 to 3A-79 do not correspond exactly to the amino acids of SEQ ID NO:1 or SEQ ID NO:2. This is because not every amino acid residue will be distinguishable from the X-ray diffraction data and so may not appear with the coordinates of Figures 3 and 3A-1 to 3A-79. For example, terminal amino acids are commonly not distinguishable from X-ray diffraction data due to their high mobility. Further, the electron densities corresponding to the long side chains of some amino acids may not be visible. This observation is common in the art of protein crystallography and is referred to as disorder. Thus for the purpose of modeling, an alanine is often inserted artificially at those positions where atoms beyond the beta carbon of a residue are disordered (compare, for example,

the arginine at position 70 in ACPS molecule A1 in Figure 3A-9 (consistent with the residue at the same position in SEQ ID NO:2) with the alanine at position 70 in ACPS molecule B1 in Figure 3A-25). The sequences of the three ACPS molecules in Figures 3 and 3A-1 to 3A-47, and of the three ACP molecules in Figures 3A-47 to 3A-79 are not inconsistent, and the claims have been amended to specifically reference the sequences set forth in SEQ ID NO:1 and SEQ ID NO:2. The claims are therefore not indefinite.

Claims 39-48 were amended to have proper antecedent basis.

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejection of claims 2-5, 9-13, and 34-48 under 35 U.S.C. § 112, second paragraph.

Written Description. The Examiner rejected claims 1-7 and 34-48 under 35 U.S.C. § 112, first paragraph for lack of written description, alleging that "[w]hile the structure of one species of said genera of crystallized complexes is disclosed in the specification, structural and functional limitations adequate to describe the instant genera of crystallized complexes are lacking." *See* Office Action at page 9. Claim 1 has been amended to specify that the crystallized complex belongs to space group $C222_1$. Recitation of the space group sufficiently characterizes the structure of the crystallized complex to satisfy the written description requirement. *See* Case 4 of the Trilateral Report on Protein 3D Structure Related Claims at pages 33 and 67.

The Examiner also rejected claims 9-13 for lack of written description. Claims 9-13 have been canceled, and therefore this rejection is moot.

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of written description.

Enablement. The Examiner rejected claims 1-7 and 34-48 under 35 U.S.C. § 112, first paragraph for lack of enablement. In *In re Wands* 858 F.3d 731 (Fed. Cir. 1998), the United States Court of Appeals for the Federal Circuit described the factors to be considered and balanced when determining whether a disclosure satisfies the enablement requirement. The Wands factors are discussed below.

The breadth of the claims:

The subject matter covered by the claims is no broader than Applicants' contribution.

The nature of the invention:

The invention generally relates to a crystallized complex including ACPS and ACP and belonging to space group $C222_1$.

The state of the prior art:

No one has previously disclosed or suggested the crystallized complexes covered by the pending claims.

The level of one of ordinary skill in the art:

In general, one of ordinary skill in the art of protein crystallography would likely have an advanced degree in biology (*e.g.*, protein biology) or a related field, and possible additional experience.

The level of predictability in the art:

The relevant art is generally unpredictable. However, the present application discloses sufficient information to allow one of ordinary skill in the art to successfully make the crystallized complexes covered by the claims with a reasonable degree of predictability.

Guidance and working examples:

Applicants disclose a working example that describes the generation of a complex containing ACPS and ACP, and the crystallization of this complex. *See* Application at page 19 *et seq.* (Example 1). Applicants' guidance is sufficient to enable one of ordinary skill in the art of protein crystallography to make a crystallized complex containing ACPS and ACP and belonging to space group $C222_1$.

The amount of experimentation required:

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *See,* M.P.E.P. §2164.01 citing *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.* As discussed above, Applicants have disclosed a crystallized complex containing ACPS and ACP and belonging to space group $C222_1$. *See* Application at page 19 *et*

seq. (Example 1). Accordingly, the quantity of experimentation needed to make and use the invention is not undue.

The Examiner also rejected claims 9-13 for lack of enablement. Claims 9-13 have been canceled, and therefore this rejection is moot.

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejection for lack of enablement under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 101

The Examiner rejected claims 9-13 under 35 U.S.C. § 101. Claims 9-13 have been cancelled, and therefore the rejection is moot.

35 U.S.C. § 102

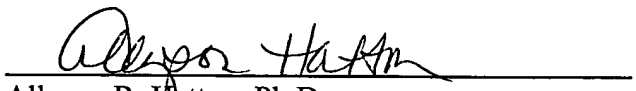
The Examiner rejected claims 9-12 under 35 U.S.C. § 102. Claims 9-12 have been cancelled, and therefore the rejection is moot.

Applicants believe the application is in condition for allowance, which action is requested.

Enclosed is a $120 check for the fee for a Petition for Extension of Time for one month. Please apply any other charges or credits to Deposit Account No. 06 1050, referencing Attorney Docket No. 16163-031002.

Respectfully submitted,

Date: November 2, 2005



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